UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ROLF W. PFIRRMANN

Appeal No. 2006-0212
Application No. 09/527,558

ON BRIEF

Before SCHEINER, MILLS and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to methods of preventing thrombosis in a liquid delivery system such as a catheter using a combination of taurolidine or taurultam and an anticoagulant. The examiner has rejected the claims as obvious in view of the prior art. We have jurisdiction under 35 U.S.C. § 134. We reverse in part, vacate in part, and enter a new ground of rejection.

Background

"Delivery systems are widely used in medicine for introducing liquid material which might include medicaments, nutrition or other active agents to a patient. . . . Typical systems include central catheters such as may be used for total parenteral

nutrition . . . and subcutaneously implanted port systems such as may be used in the treatment of malignant conditions." Specification, page 1.

"One problem associated with the use of liquid delivery systems, e.g., port or catheter-based systems, is that these can give rise to infections which in turn may lead to infected intra-atrial thrombus. . . . One solution to this problem is the use of solutions containing the antibacterial agents taurolidine and/or taurultam. . . . [I]n WO98/28027, taurolin solutions have been suggested for use as a temporary seal or flush to prevent or reduce sepsis in port systems or catheters." Pages 1-2. Taurolin is apparently a trade name for taurolidine. See Lehner,[1] page 9, line 20.

The specification discloses a "procedure to prevent deposits of thrombosis of fibrin and/or fibrin/collagen nets by combined application of taurolidine and/or taurultam in suitable isotonic or hypertonic solutions with added anticoagulant. This procedure serves to prevent catheter-sepsis and serious consequences for the patient. Also this combination serves to prevent catheter-blockage, thus avoiding risky surgical intervention for removal of thrombotic plugs . . . or a change of catheters." Pages 3-4.

Discussion

1. Claim construction

Claims 1-4, 13, and 24-34 are pending and on appeal. Claims 1 and 24 are representative and read as follows:

> 1. A method of preventing thrombosis formation on a liquid-containing surface of a liquid delivery system, the liquid delivery system being connected to a patient for delivery of a liquid to said patient, the method comprising forming a seal in the liquid delivery system between delivery of liquids using a thrombosis-preventing liquid containing taurolidine,

[1] Lehner, WO 98/28027, published July 2, 1998.

taurultam or a mixture thereof, said thrombosis-preventing liquid further containing an anticoagulant agent other than taurolidine or taurultam.

24. A method of preventing thrombosis formation on a liquid-containing surface of a liquid delivery system, the liquid delivery system being connected to a patient for delivery of a liquid to said patient, the method comprising first contacting said surface with a solution containing a thrombosis-preventing amount of an anticoagulant agent other than taurolidine or taurultam, thereafter contacting said surface with a solution containing taurolidine, taurultam or a mixture thereof, and repeating both of the surface contacting steps between delivery of liquids to said patient.

Thus, claim 1 is directed to a "method of preventing thrombosis [sic, thrombus?] formation on a liquid-containing [sic, contacting?] surface of a liquid delivery system," comprising "forming a seal" in between times of liquid delivery, using a composition containing taurolidine or taurultam and an anticoagulant agent other than taurolidine or taurultam. The specification makes clear that "forming a seal" in a liquid delivery system means filling the system with the recited composition. See page 6, lines 12-16 ("Should there be any period of time when it is desired not to use the delivery system for administration . . . , the delivery system can be filled with a solution in accordance with the invention to act as an antimicrobial seal.").

Claim 24 is directed to a "method of preventing thrombosis [sic, thrombus?] formation on a liquid-containing [sic, contacting?] surface of a liquid delivery system," comprising first contacting the surface with a solution containing an anticoagulant other than taurolidine or taurultam, then contacting the surface with a solution containing taurolidine or taurultam, and repeating both steps.

2. Obviousness over Lehner, Raad, and Ito

The examiner rejected claims 24-34 under 35 U.S.C. § 103 on the basis that the claimed subject matter would have been obvious in view of Lehner, Raad,[2] and Ito.[3] The examiner characterized Lehner as "teach[ing] repeating the step of contacting or flushing with taurolidine or taurultam, but not with another anticoagulant agent. See page 10, lines 4-12." Examiner's Answer, page 5. The examiner cited Raad as "teach[ing] that prophylactic flushing of a catheter with heparin to prevent [thrombotic occlusion] is the standard of care . . [and] that other known anticoagulants, such as citrate and hirudin, have utility in antithrombotic prophylaxis." Id. The examiner cited Ito merely for its disclosure of specific anticoagulants. See the Examiner's Answer, page 6.

The examiner concluded that

> [i]t would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the LEHNER process by first flushing the liquid-delivery system with an anticoagulant, as is the standard of care taught by RAAD. . . . It would have been within the scope of the artisan to select any known thrombogenesis inhibitor for this purpose.

Examiner's Answer, pages 6-7.

Appellant argues that the cited references do not teach or suggest the repeated two-step process recited in claim 24. See the Appeal Brief, pages 12-13.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." In re

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[2] Raad et al., U.S. Patent 5,688,516, issued November 18, 1997.
[3] Ito et al., U.S. Patent 5,167,960, issued December 1, 1992.

Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). "[I]dentification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant." In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000).

We agree with Appellant that the cited references, viewed without the benefit of hindsight, would not have suggested the method of claim 24 to a person of ordinary skill in the art. In our view, the examiner has not accurately characterized the teachings of Lehner. The passage cited by the examiner reads as follows:

> After each treatment with medication, . . . the delivery system is rinsed meticulously with 10 ml of a sterile 0.9% sodium chloride solution. 2 ml of a 2% Taurolin® solution are then introduced into the chamber and the needle removed. The port system is then effectively sealed against microbial infection. After being rinsed with saline, further medication may then be introduced when desired and the cycle repeated.

Lehner, page 10, lines 4-12.

The examiner characterizes this passage as "teach[ing] repeating the step of contacting or flushing with taurolidine or taurultam," but the process taught by Lehner differs significantly from that required by the claims. Claim 24 requires contacting with anticoagulant solution, then contacting with taurolidine or taurultam, and "repeating both of the surface contacting steps between delivery of liquids to said patient." While Lehner states that the taurolidine-contacting step can be repeated, the repetitions are disclosed to be with each cycle of administering medication; there is no suggestion in

Lehner to contact the port system with taurolidine repeatedly in between each administration of medication.

The examiner has pointed to no other disclosures in the cited references as a basis for concluding that the repeated two-step process recited in claim 24 would have been obvious to a person of ordinary skill in the art. Therefore, we conclude that the examiner has not made out a prima facie case of obviousness with respect to the claimed process. The rejection of claims 24-34 over the combined teachings of Lehner, Raad, and Ito is reversed.

The examiner also rejected claims 24-34 under 35 U.S.C. § 103 as obvious in view of Lehner and Raad, without Ito. That rejection is also reversed for the reason discussed above.

3. Obviousness based on Lehner and Reinmüller

The examiner rejected claims 1-4 and 13 under 35 U.S.C. § 103 as obvious in view of Lehner and Reinmüller.[4] See the Examiner's Answer, pages 3-5. While these references might support a prima facie case obviousness, we believe that Lehner and Raad represent the closest prior art to the claimed method.

We therefore vacate the rejection of claims 1-4 and 13 based on Lehner and Reinmüller.

[4] Reinmüller, U.S. Patent 5, 077,281, issued December 31, 1991.

4. New ground of rejection

Under the provisions of 37 CFR § 41.50(b), we enter the following new ground of rejection: claims 1-4 and 13 are rejected under 35 U.S.C. § 103 as obvious in view of Lehner and Raad. Lehner teaches a method of preventing bacterial infections in catheter- or port-based liquid delivery systems, comprising sealing the delivery system with a solution of taurolidine or taurultam between times of medication delivery. See, e.g., page 6, lines 32-36 and page 10, lines 4-12.

Lehner does not teach sealing a catheter- or port-based system with a composition containing taurolidine or taurultam in combination with another anticoagulant. However, Raad teaches that "vascular catheters have become the major source for hospital-acquired sepsis. . . . Thrombotic occlusions of the lumen of central venous catheters (CVC) is another complication that will often lead to the removal of catheters." Column 1, lines 28-35. Raad states that the "standard of care of catheters includes flushing the lumen of the catheter with heparin. However, heparin has no antimicrobial activity. Thus, infections, as well as thrombotic occlusions, continue to occur frequently despite the prophylactic use of heparin flushes." Column 1, lines 36-40.

Raad discloses that a combination of a "non-glycopeptide antimicrobial agent . . . and a chelating agent, anticoagulant or antithrombotic agent" is useful for "maintaining catheter patency"; that is, preventing thrombotic occlusion of a catheter. See column 4, lines 30-35 and column 6, lines 20-23. In particular, see column 8, lines 47-54:

> The present invention also provides a method for inhibiting glycoprotein-rich glycocalyx formation at a catheter port. The method in one embodiment comprises flushing the catheter periodically with a

> pharmaceutical preparation comprising a glycocalyx-inhibiting concentration of a chelating agent, an anticoagulant or an antithrombotic agent, and a non-glycopeptide antimicrobial agent, in a pharmacologically acceptable carrier solution.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method taught by Lehner of sealing a catheter- or port-based liquid delivery system, between times of medication delivery, by adding an anticoagulant to Lehner's taurolidine- or taurultam-containing solution. Motivation to do so is provided by Raad, who teaches that the combination of an antimicrobial compound and an anticoagulant is beneficial in preventing thrombotic occlusion of catheters, which leads to infection. See column 2, lines 40-51. Lehner teaches that taurolidine and taurultam are antimicrobial agents (page 6, lines 16-20); hence, those skilled in the art would have been led by Raad to modify Lehner's method by adding an anticoagulant to the solution used to seal the catheter- or port-based system. Thus, the disclosures of Lehner and Raad would have suggested the method of claim 1 to a person of ordinary skill in the art.

Lehner and Raad also would have rendered obvious claims 2-4 and 13.[5] Lehner teaches maintaining contact of the taurolidine with the surface for a minimum of one hour, "though the seal can be retained for up to twelve hours or more." Page 7, lines 10-12. Lehner teaches that a "preferred solution will contain from 0.5 to 3% by weight of taurolidine, or from 1 to 7.5% by weight of taurultam." Page 7, lines 34-36. Finally,

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[5] Claim 2 depends on claim 1 and adds the limitation that the composition is contacted with the surface for at least an hour. Claim 3 depends on claim 2 and raises the time period to at least 12 hours. Claim 4 depends on claim 3 and adds the limitation that the composition is replaced at least about daily. Claim 13 depends on claim 1 and adds the limitation that the composition contains from about 0.5 to about 3% by weight of taurolidine, or from about 1 to about 7.5% by weight of taurultam.

Lehner teaches sealing a catheter-based system used for parenteral nutrition delivery in between nightly feeding cycles. These disclosures reasonably appear to suggest the additional limitations of claims 2-4 and 13.

Summary

We reverse the examiners' rejection of claims 24-34, and vacate the examiner's rejection of claims 1-4 and 13 in favor of a new ground of rejection based on Lehner and Raad.

Time Period for Response

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution*. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .

(2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

REVERSED-IN-PART, VACATED-IN-PART, 37 CFR § 41.50(b)

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